JOURNAL OF CLINICAL MICROBIOLOGY, June 2006, p. 2158–2159 Vol. 44, No. 6
0095-1137/06/$08.00+0 doi:10.1128/JCM.02358-05

Detection of Carcinogenic Human Papillomavirus in Specimens Collected with a Novel Self-Sampling Device

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Received 10 November 2005/Returned for modification 9 January 2006/Accepted 10 April 2006

We compared the detection of carcinogenic human papillomavirus DNA in cervicovaginal specimens self-collected using a novel device to the detection in physician-collected cervical specimens from 137 women. The kappa value was 0.66 (95% confidence interval, 0.53 to 0.78), with an 83% overall test agreement and a 68% positive test agreement.

Based on the central role of carcinogenic human papillomavirus (HPV) types in the development of cervical cancer (1, 3, 7) and its immediate precursor lesions (5), HPV testing has now been approved in the United States as an adjunct to cytology for triage at all ages and for general screening in women aged 30 years and older (8). One possible method to expand HPV-based cervical cancer screening to underserved populations is self-collection of cervicovaginal specimens. Numerous studies have evaluated self-collection in combination with HPV DNA testing as a potential alternative to cytology in low-resource settings. A new device (1a) was designed to physically mimic tampons and perhaps improve sampling of the cervix while minimizing sampling of the vagina. The self-sampling device has an ejectable tip, which is protected during insertion and removal by a retractable outer sheath. In this pilot validation study, we compare the detection of carcinogenic HPV DNA in cervicovaginal specimens self-collected using the Fournier device to detection in cervical specimens collected from the cervix by a physician.

MATERIALS AND METHODS

The study was carried out at the Department of Obstetrics and Gynecology Division of Gynecologic Oncology at the University of Miami School of Medicine. The institutional review board of the university approved the study. In total, 146 nonpregnant, nonhysterectomized women were recruited from the colposcopy and general gynecology clinics at Jackson Memorial Hospital, and 137 women (94%) agreed to participate and provided written, signed, informed consent. A research nurse assigned to the study explained the use of the self-sampling device (Fournier device) to the study subjects. A video demonstration was also shown to the study participants. Upon completion of the self-collection, women underwent a standard pelvic examination during which cervical specimens were collected using plastic disposable specula, cytobrushes, and Ayer's spatulas.

The tip of the self-sampling device was ejected into a vial containing a liquid-based cytology medium (SurePath; TriPath, Burlington, NC) and vortexed to release cells. Cytobrushes and Ayer's spatulas were immersed and agitated in a separate vial containing the SurePath medium to release cells. Specimens were then processed for the production of cytology slides according to the manufacturer's specifications.

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HPV DNA testing. A Hybrid Capture 2 (HC2) (Digene Corporation, Gaithersburg, MD) test, a pooled-probe DNA test for one or more carcinogenic HPV types (HPV16, -18, -31, -33, -35, -39, -45, -51, -52, -56, -58, -59, and -68) (4), with probe set B was performed on residual SurePath specimens as previously described (6).

Statistical analysis. We calculated kappa values, overall agreement, and positive agreement with 95% confidence intervals (95% CI). McNemar's χ^2 test was used to test for statistical differences ($P < 0.05$) in HC2 positive test results between physician-collected and self-collected specimens. We also compared the paired HC2 results of the self-collected specimen and the physician-collected specimen to the cytology results from the physician-collected specimens.

RESULTS

Of 137 patients enrolled, 135 (99%) had complete data and were included in this analysis. One-third (33%) of the women in the study sample were younger than 30 years of age and 18% were older than 49. Women were predominately African-American (44%) or Caucasian (49%). Two-thirds of the participants had completed high school or attended college, while 25% did not have any formal education.

Table 1 summarizes the results of the HPV DNA testing of specimens collected by the two methods. Sixty-one physician-collected samples (45%) and 58 patient-collected samples (43%) tested positive by HC2 ($P = 0.5$, McNemar's χ^2). The kappa value for the HC2 test results on the paired specimens was 0.66 (95% CI, 0.53 to 0.78), with an 83% overall agreement and a 68% positive agreement.

A comparison of cytology and paired HC2 test results for physician-collected and patient-collected specimens is shown in Table 2. There was 75%, 100%, 83%, and 78% concordance of HC2 results for women with high-grade squamous intraepithelial lesions (HSIL), low-grade squamous intraepithelial lesions (LSIL), atypical squamous cells of undetermined significance (ASCUS), and negative cytology, respectively. Two (50%) of 4 patients with HSIL cytology, 22 (88%) of 25 with LSIL cytology, 11 (37%) of 30 with ASCUS cytology, and 13 (17%) of 76 with negative cytology were HC2 positive for both physician-collected and patient-collected specimens. Of the remaining two HSIL cases, one tested HC2 positive for the physician-collected specimen but negative for the patient-collected specimen and the other tested negative by HC2 for both specimens.

TABLE 1. Paired HC2 test results for physician-collected cervical specimens and self-collected cervicovaginal specimens collected using the Fournier sampler[a]

Result for physician-collected specimen	No. (%) of self-collected specimens that tested:		Total
	Negative	Positive	
Negative	64 (86)	10 (14)	74
Positive	13 (21)	48 (79)	61
Total	77	58	135

[a] Kappa, 0.66 (95% CI, 0.53 to 0.78); agreement, 83.0% (95% CI, 75.5 to 88.9); positive agreement, 67.6% (95% CI, 55.5 to 78.2%); $P = 0.5$ (McNemar's χ^2).

TABLE 2. Comparison of paired HC2 results to liquid-based cytology (SurePath) interpretations[a]

Result for physician-collected specimen	No. (%) of physician/self-collected specimens that tested:				Total	*P*
	Negative/ negative	Positive/ negative	Negative/ positive	Positive/ positive		
Negative	46 (61)	9 (12)	8 (11)	13 (17)	76	0.8
ASCUS	14 (47)	3 (10)	2 (7)	11 (37)	30	0.7
LSIL	3 (12)	0 (0)	0 (0)	22 (88)	25	1
HSIL	1 (25)	1 (25)	0 (0)	2 (50)	4	0.3
Total	64 (47)	13 (10)	10 (7)	48 (36)	135	0.5

[a] The differences in HC2 test results within each cytology category were tested for statistical differences by using McNemar's χ^2 test.

DISCUSSION

We found a good concordance between test results of HC2, an FDA-approved test for carcinogenic HPV DNA, performed on cervicovaginal specimens self-collected using the Fournier device and physician-collected cervical specimens. Although this was a small sample of women, we suggest that this device might offer an acceptable alternative to the relatively uncomfortable and costly traditional collection method of undergoing a pelvic exam for the collection of a cervical specimen. Self-sampling can potentially reduce the patient time and travel, with only women who test positive needing additional clinical follow-up.

We note a couple of limitations for this pilot study. First, our limited sample size in this pilot study prevented us from assessing the clinical performance for detection of histologically confirmed precancer and cancer. The small number of HSILs, a less rigorous outcome, did not permit us to assess the relationship between HPV testing of self-collected samples and HSIL cytology. Second, we did not alter the order of specimen collection, which could have introduced a systematic bias and reduced concordance of HPV test results between the two specimens.

In summary, the good concordance with HPV DNA detection with the referent standard, the cervical specimen collected by the physician, and its acceptability suggest that the Fournier device may be a useful device for self-collection. However, larger studies that include rigorous histologic endpoints and follow-up to overcome the insensitivities of colposcopy (2) are clearly needed to validate this device for screening. This device is more complicated and expensive than using a simple Dacron swab or even a tampon for self-sampling, and increased performance and acceptability must be demonstrated to warrant its use. Finally, cost utility analyses will also be needed to assess the viability of using this device in primary cervical cancer screening.

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